10

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,407	09/22/2003	Denise N. Haefliger	2590-87	4475

23117 7590 07/15/2004

NIXON & VANDERHYE, PC
1100 N GLEBE ROAD
8TH FLOOR
ARLINGTON, VA 22201-4714

EXAMINER
SALIMI, ALI REZA

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,407	HAEFLIGER ET AL.	
	Examiner	Art Unit	
	A R Salimi	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/288,861.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt of preliminary amendment of 9/22/2003, is acknowledged. Claims 1-19 have been canceled. Claims 20-39 have been added and are pending.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). Please update the current information status.

Claim Rejections - 35 USC § 112

Claims 20-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is vague and indefinite, the intended metes and bounds of the attenuated Salmonella strain(s) is are not defined. In addition, the claim is indefinite for recitation of "viable", this is a relative terminology, and how can one determine whether the vaccine is "viable"? The claim has been interpreted in light of specification and since the specification does not provide what is intended by "viable" vaccine, the claim is considered to be vague and indefinite. The claim has been interpreted in light of the specification and since the specification asserts that not every mutation would form a viable attenuated salmonella strain the claim is indefinite. This affects the dependent claims.

Claim 37 recites the limitation "wherein the HPV L1 major capsid protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 38 recites the limitation "wherein the HPV L1 major capsid protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 39 recites the limitation "wherein the HPV L1 major capsid protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

Claims 20-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for attenuated Salmonella strain selected from the groups consisting of mutation in the PhoP/PhoQ and ∆cya, ∆cyp ∆cdt, does not reasonably provide enablement for nay and all attenuated Salmonella strain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The specification is deficient in providing teaching for any and all attenuated Salmonella strain suitable for use in a live vaccine. The specification provides teaching that some of the attenuated Salmonella caused fever and some induced low level antibodies (see for example page 5 of the specification). Yet, the scope of the claims refers to any and all types of attenuated salmonella stain capable of use as a live vaccine. This should be reconciled. The state of the art is very unpredictable and absent Applicants teaching undue experimentation would be required to enable the full scope of the invention. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be

required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Please note the examiner is aware of the limitation of "prophylaxis" in claim 15 of The U.S. Patent No. 6,251,406. However, this limitation appears to be in error and it does not reflect the changes made in the Examiner's Amendment in order to place the application in condition for allowance, and which the attorney of record authorized. Hence, the rejection below is not inconsistent with Office's position.

Claim Rejections - 35 USC § 112

Claims 20-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the utilization of a live vaccine in treating papillomavirus, does not reasonably provide enablement for utilization of the live vaccine as a prophylactic or prophylaxis of human or animal against papillomavirus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The limitation is reserved for eradication of a disease or prevention of disease or of a prevention of a process that can lead to a disease. Applicants are reminded that although the literature now supports the notion of therapeutic vaccine wherein the vaccine comprises L1 protein of human papillomavirus (HPV) to induce a therapeutic response against the said virus, the literature to date does not support the prophylactic vaccine for protection of human papillomavirus before the onset of the infection (see Fife K., Australasian Journal of Dermatology, 1998, vol. 39 Suppl 1S8-10, see the abstract, and page S9,

right column). The state of the art regarding a prophylactic vaccine for HPV does not even support as to how the HPV infects cells, or whether antibody alone is sufficient to induce protection or whether CTL is required, this should be reconciled. Applicants are more than welcome to provide evidence of pre or post filing that provide the state of the art showing prophylactic vaccine results directed against HPV are well established and are routine. In essence, the prophylactic vaccine of the invention claims that an individual who is not yet infected with HPV may receive a dose of the applicants' composition prior to the onset of the human papillomavirus and at sometime in the future when and if that individual becomes infected with human papillomavirus the individual would induce a sufficient and appropriate immune response to eliminate the virus and completely protect the individual from infection. This has not been shown or taught by the disclosure. The specification has not provided adequate teaching regarding a prophylactic vaccine. There is no teaching as to what type of immune response would be required or is induced for a sufficient prophylactic response, whether a Th1 or Th2 response is required, these are not simple issues that can be glossed over. The specification provides no teaching with said regard. This is a very unpredictable filed, and absent teaching it would require undue experimentations to enable the full scope of the claimed invention. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988)*.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,251,406 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap in scope.

Claims 20-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,458,368 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap in scope.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hopkins et al (Infection And Immunity, 1995, pp. 3279-3286), and Kirnbauer et al (J of Virology, 1993, pp. 6929-6936).

The claims are directed to utilization of attenuated prokaryotic microorganism transformed cell by nucleic acid of papillomavirus capsid nucleic acid.

Hopkins et al disclosed the employment of Salmonella typhimurium strain (Phop) carrying hepatitis B virus core antigen wherein the antigens induce d antibodies (see the abstract). This differs form the claims since they did not used papillomavirus antigens.

Kirnbauer et al disclosed L1 major capsid protein of papillomavirus self assembles into a virus like particles, and they disclosed coexpression of HPV16 L1 plus L2 utilizing baculovirus vector. This differs since they did not use prokaryotic expression system.

However, one of ordinary skill in the art at the time of filing would have been highly motivated by the above teaching to include the L1 protein as taught by Kirnbauer et al into the expression system taught by Hopkins et al. The ordinary skill in the art being familiar with state of the art would not have anticipated any unexpected results. In addition, certain limitations such as fusion of the proteins and method of utilizing the proteins in a method of detection are seen as notoriously obvious in this art, unless the proof of criticality is proven. Therefore, the invention as a whole is seen as prima facie obvious absent unexpected results.

Claims 20-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Londono et al (Vaccine, 1996, vol. 14, pp.545-552), and Kirnbauer et al (J of Virology, 1993, pp. 6929-6936).

Londono et al disclosed an attenuated Salmonella typhimurium strain expressing chimeric E7 papillomavirus protein (see the abstract, and page 546, left column first full paragraph). This differs since they not use the capsid protein.

Kirnbauer et al disclosed L1 major capsid protein of papillomavirus self assembles into a virus like particles, and they disclosed coexpression of HPV16 L1 plus L2 utilizing baculovirus vector. This differs since they did not use prokaryotic expression system.

Therefore, one of ordinary skill in the art at the time of filing would have been highly motivated by the above teaching to include the L1 protein as taught by Kirnbauer et al into the

expression system taught by Londono et al. The ordinary skill in the art being familiar with state of the art would not have anticipated any unexpected results. In addition, certain limitations are seen as obvious and purview of one of ordinary skill in the art. Therefore, the invention as a whole is seen as prima facie obvious absent unexpected results.

Claims 20-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fouts et al (Vaccine, 1995, vol. 17, pp.1697-1705), and Kirnbauer et al (J of Virology, 1993, pp. 6929-6936).

Fouts et al disclosed the construction Salmonella typhimurium as vectors capable of expressing HIV-1 gp120 protein and induction of immune response. This differs form the claims since they did not used papillomavirus antigens.

Kirnbauer et al disclosed L1 major capsid protein of papillomavirus self assembles into a virus like particles, and they disclosed coexpression of HPV16 L1 plus L2 utilizing baculovirus vector. This differs since they did not use prokaryotic expression system.

Therefore, one of ordinary skill in the art at the time of filing would have been highly motivated by the above teaching to include the L1 protein as taught by Kirnbauer et al into the expression system taught by Fouts et al. It would have been obvious to substitute one gene for another without expectation of unexpected result. The ordinary skill in the art being familiar with state of the art would not have anticipated any unexpected results. In addition, certain

limitations are seen as obvious and purview of one of ordinary skill in the art. Therefore, the invention as a whole is seen as prima facie obvious absent unexpected results.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (571) 272-0909. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (571) 272-0902. The Official fax number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

A. R. Salimi

7/7/2004